MIC

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TI Diterpenoids from the roots of Salvia sclarea.
AU Ulubelen, Ayhan (1); Sonmez, Ufuk (1); Topcu, Gulacti
CS (1) Fac. Pharm., Univ. Istanbul, 34452 Istanbul Turkey
SO Phytochemistry (Oxford), (1997) Vol. 44, No. 7, pp. 1297-1299.
ISSN: 0031-9422.
DT Article
LA English

TI 2-BETA HYDROXYHAUTRIWAIC-ACID A CLERODANE TYPE DITERPENOID AND OTHER TERPENOIDS FROM THREE BACCHARIS SPECIES.
AU ARRIAGA-GINER F J; WOLLENWEBER E; SCHOBER I; DOSTAL P; BRAUN S
CS DEPARTAMENTO DE QUIMICA ORGANICA, UNIVERSIDAD AUTONOMA DE MADRID, CANTO
BLANCO, E-28034 MADRID, SPAIN.
SO PHYTOCHEMISTRY (OXF), (1986) 25 (3), 719-722.
CODEN: PYTCAS. ISSN: 0031-9422.
FS BA; OLD
LA English

TI Diterpenes from the genus Amaracus
AU Passannanti, Salvatore; Paternostro, Mariapia; Piozzi, Franco; Barbagallo, Claudia
CS Inst. Org. Chem., Univ. Palermo, Palermo, Italy
SO Journal of Natural Products (1984), 47(5), 885-9
CODEN: JNPRDF; ISSN: 0163-3864
DT Journal
LA English

TI A DITERPENE AND FLAVONOIDS OF BACCHARIS-FLABELLATA.
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SO PHYTOCHEMISTRY (OXF), (1988) 27 (6), 1884-1887.
CODEN: PYTCAS. ISSN: 0031-9422.
FS BA; OLD

(MeOH). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3460, 3490 (OH); 1505, 880 (furan ring); 1743, 1720 (lact ne); 1630 (double bond); UV λ_{max}^{MeOH} nm: 215 (furan ring). ^{1}H NMR (300 MHz, acetone-d_6 and acet ne-d_6 plus D_2O): see Results and Discussion; Overhauser effect, irradiation at C-5 methyl group resulted in 11.1% NOE f C-10 hydroxyl while irradiation at C-10 hydroxyl resulted in 8.3% NOE of C-5 methyl (see Fig. 1) ^{13}C NMR (75.43 MHz, acetone-d_6): Table 1. High resolution MS: 374.133 [M]$^+$, (20%, calc. for $C_{20}H_{22}O_7$: 374.1326), 124.0875 (100%, calc. for $C_8H_{12}O$: 124.0888), 95.0492 (22%, calc. for C_6H_7O: 95.0496), 94.0417 (41%, calc. for C_6H_6O: 94.0418), 81.0345 (45%, calc. for C_5H_5O: 81.0340).

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A DITERPENE AND FLAVONOIDS OF *BACCHARIS FLABELLATA*

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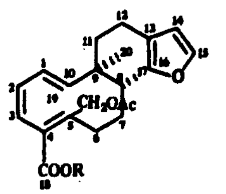
Key Word Index—*Baccharis flabellata*; Compositae; *seco*-clerodane diterpenoid; *neo*-clerodane diterpenoid; oleanolic acid; flavonoids.

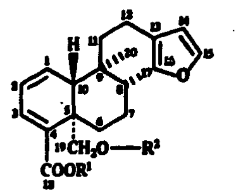
Abstract—From the aerial parts of *Baccharis flabellata*, two new clerodane type diterpenes were isolated together with oleanolic acid and four known flavonoids. The structures of the new compounds were elucidated by spectroscopic methods.

INTRODUCTION

Following our chemical study of the genus *Baccharis* (C mpositae) [1–7], we have now investigated the constituents of *B. flabellata*. From the aerial parts f this plant we have isolated a new 5,10-*seco*-clerodane diterpen id derivative, together with oleanolic acid and the four foll wing flavonoids: 5,7,4′trihydroxy-6,3′-dimethoxyflavone (jaceosidin); 5,3′,4′-trihydroxy-6,7-dimethoxyflavone (cirsiliol); 5,7,3′,4′-tetrahydroxy-6-methoxyflavone (nepetin); 5,7,4′-trihydroxy-6-methoxyflavone (hispidulin). This paper describes the structural elucidation of the new compounds.



	R
1a	H
1b	Me



	R^1	R^2
2a	H	Ac
2b	Me	Ac
2c	H	H

DISCUSSION

The HRMS of compound **1a** provided the molecular formula $C_{22}H_{28}O_5$. Its IR spectrum showed the presence of a carboxyl group (3400–2500 cm^{-1}), an ester group (1740, 1260 cm^{-1}), olefinic bonds and a furan ring (3100, 1630, 1500, 875, 780 cm^{-1}). On treatment with diazomethane compound **1a** afforded **1b**. The ^{1}H NMR of **1b** revealed the existence of a β-substituted furan ring due to the typical resonance pattern arising from three aromatic protons at δ6.36, 7.46 and 7.36 (Table 1). In addition, the mass spectrum exhibited the expected peaks for a β-ethyl furan side chain at m/z 95 and 81 (base peak) and the ^{13}C NMR spectrum showed signals at δ125.2, 110.5, 138.0 and 142.0, assigned to C-13, C-14, C-15 and C-16, respectively, of the assumed β-ethyl furan side chain [8]. The ^{1}H NMR spectrum also showed signals for a carboxymethyl group as a singlet at δ3.71, an acetoxymethylene group which appeared as a narrowly double doublet at δ3.78, and a methyl signal at δ2.09. It also showed two methyl groups, a secondary one at δ0.83 and a tertiary at δ0.73. The presence of a methine attached methyl group, which is a frequent feature at C-8 among clerodane-like diterpenes, suggested that **1a** might belong to this class of natural products.

The olefinic proton signal pattern sh wed a narrow *dd* at δ7.13, a *ddd* at 5.90, a *ddd* at 5.55 and a *dd* at 5.26. These four signals must be attributed to the existence of a triene olefinic system, which can nly be accommodated in a 5,10-*seco*-clerodane skeleton as described in **1a**. The MS (M^+ at m/z 386) and the ^{13}C NMR spectrum agreed with the proposed structure **1a**.

A diagram of the olefinic part of the ^{1}H NMR spectrum of **1b** was reproduced through a program by the spectrum simulator of the Lawrence University (Program NMRSIM, version 1c, 13 December 1974 by R. James S. Evans, Department of Chemistry, Lawrence University).

The ^{13}C NMR spectrum also defined the relative stereochemistry at C-8 and C-9 by comparison of the δ values of the C-17 and C-20 methyl groups with those described for related clerodane diterpenes [9–11]. The values are in agreement with an equatorial methyl group at C-8 as described in **1a**.

The other furane diterpenoid **2a** had a molecular formula $C_{22}H_{28}O_5$. Its IR and mass spectra (See Experimental), ^{1}H NMR (Table 1) and ^{13}C NMR (Table 2) spectra showed a β-substituted furan ring. Furthermore, the IR spectrum showed the presence of carboxyl (3300–3600 cm^{-1}) and ester (1740, 1260 cm^{-1}) groups. On treatment with diazomethane, compound **2a** afforded **2b**, which showed in the ^{1}H NMR spectrum a carboxymethylene group which was observed as an AB system at δ4.43 and 4.13 with the characteristic geminal coupling constant between the methylene protons (10 Hz) and the singlet methyl signal at 1.95. The chemical shift value of the tertiary and secondary methyl groups were near to those of H-17 and H-20 in **1a** and suggested that **2a** might belong also to the clerodane-like diterpenoid group. A broad triplet at δ6.96 was assigned to a β-olefinic proton (H-3) conjugated with a carboxyl ester group. Two olefinic protons at δ6.17 were assigned to H-1 and H-2 that showed magnetic equivalence. A broad singlet at δ2.58 was ascribed to the H-10 proton. Spin decoupling experiments confirmed coupling between H-10 and H-1. The small value of the constant suggested a dihedral angle near 90°.

Table 1. ^{1}H NMR spectra of compounds **1b**, **2a**, **2b** and **2c**

H	1b	2a	2b	2c
1	5.55 *ddd*	6.20 *br s*	6.17 *br s*	6.16 *br s*
2	5.90 *ddd*			
3	7.13 *dd*	7.16 *br t*	6.96 *br t*	6.70 *br t*
10	5.26 *dd*	2.60 *br s*	2.58 *br s*	2.60 *br s*
14	6.36 *br s*	6.25 *br s*	6.11 *m*	6.20 *br s*
15	7.46 *m*	7.33 *m*	7.30 *m*	7.36 *m*
16	7.36 *m*	7.25 *m*	7.15 *m*	7.26 *m*
17	0.83 *d*	0.86 *d*	0.80 *d*	0.86 *d*
19	Ha 3.93 *d*;	Ha 4.44 *d*;	Ha 4.43 *d*;	
	Hb 3.63 *d*	Hb 4.13 *d*	Hb 4.13 *d*	3.80 *s*
20	0.73 *s*	0.85 *s*	0.85 *s*	0.85 *s*
COOMe	3.71 *s*	—	3.71 *s*	—
Me–CO.O	2.09 *s*	1.93 *s*	1.95 *s*	—

J (Hz) **1b**: 1,2 = 12; 1,10 = 5; 1,3 = 1; 2,3 = 1.7; 2,10 = 1.30; 19a, 19b = 9 Hz; 17,8 = 6. **2a**: 19a,19b = 10 Hz; 17,8 = 5.5. **2b**: 19a, 19b = 10 Hz; 17,8 = 5.5. **2c**: 17,8 = 5.5.

Table 2. [13]C NMR spectra of compounds **1b**, **2a** and **2b**

C	1b	2a	2b
1	142.5	136.3	134.2
2	127.9	124.7	124.7
3	126.3	135.6	133.7
10	131.8	47.9	47.8
4	119.5	134.5	135.6
5	129.8	38.2	38.1
6	35.6	30.9	30.9
7	28.3	26.8	26.8
8	35.1	35.3	35.3
9	37.9	41.0	41.0
11	37.3	37.7	37.6
12	19.2	18.7	19.6
13	125.2	124.8	124.9
14	110.5	110.6	110.7
15	138.0	138.2	138.6
16	142.0	142.5	142.5
17	13.5	15.4	15.3
18	167.1	172.4	170.8
19	62.0	62.1	62.2
20	18.1	19.7	18.0
COOMe	51.6	—	51.1
Me–CO.O	20.3	20.6	20.6
Me–C=O	170.7	170.9	167.0

The UV absorption exhibited the expected value for such a diene system (λ_{max}^{MeOH} nm 298; $\lambda_{max}^{n-hexane}$ nm 292). The [13]C NMR spectrum of this compound was in agreement with these assignments and was made on the basis of the observed multiplicities (APT) and of the comparison with reported [13]C NMR spectral data of similar derivatives [12]. The chemical shifts of C-17 and C-20, as well as those of **1a**, also defined the relative configuration of C-8 and C-9 [9–11]. The large negative optical rotation (See Experimental) suggests that the absolute configuration of **2a** was that of hautriwaic acid [12].

Finally the treatment of **2a** with methanolic KOH yielded **2c**. The spectroscopic data of the latter (1H NMR, IR and UV) led us to identify it as a clerodane, already found in *Dodonaea attenuata* [13].

EXPERIMENTAL

[13]C and [1]H NMR spectra were recorded in $CDCl_3$; M spectra were determined utilizing a Varian Mat 112 S spectrometer at 70 eV and 0.7 mA.

Plant material. *Baccharis flabellata* was collected in March and September 1985 in Tucuman and San Luis respectively. Voucher specimens are kept at the Herbaria (VMSL 2862; UNSL 34).

Extraction and isolation. The air-dried plant material (1.2 kg) was extracted with h t MeOH (3 × 3). The extract was concd t 1.5 l, then, H_2O was added (10; 20 and 30%) and partitioned between *n*-hexane, CCl_4, $CHCl_3$ and EtOAc, respectively. The $CHCl_3$ was evapd and the residue (45 gr) was subjected to CC on silica gel 60 G and devel ped successively with C_6H_6 and C_6H_6 containing increasing proportions of EtOAc. Fractions f 100 ml were taken and combined upon TLC monitoring, yielding the f llowing compounds in rder f elution: **1a** (80 mg); **2a** (500 mg); oleanolic acid (4 g) and a mixture of f ur flav noids. The mixture of flavonoids was rechromatographed first n a silica gel column (120 g) where it was eluted with C_6H_6–EtOAc (5:5) and then on a Sephadex LH-20, where it was eluted with MeOH, yielding: 5,7,4′-trihydroxy-6,3′-dimethoxy flavone; 5,3′,4′-trihydroxy-6,7-dimethoxy flavone; 5,7,3′4′-tetrahydroxy-6-methoxy flavone; 5,7,4′-trihydroxy-6-methoxy flavone. The previously known flavonoids were identified by comparison of their spectroscopic ([1]H NMR, UV and MS) properties with those reported in the literature [14, 15].

Compound **1a**. Colourless oil, IR ν_{max}^{KBr} cm^{-1}: 3400, 3100, 2500, 1740, 1630, 1500, 1260, 875, 780. HRMS calc. for $C_{22}H_{28}O_5$ MW: 372.1937, found M_r (MS) 372.1929. 80 mg **1a** were dissolved in dry Et_2O, and CH_2N_2 was added slowly, following the usual work-up to give 75 mg of **1b**, colourless oil. MS m/z (rel. int.): 386 $[M]^+$ (2); 343 (4); 326 (5); 313 (10); 295 (8); 283 (14); 231 (10); 149 (35); 95 (37); 91 (27); 81 (100). For [1]H NMR data, see Table 1. [13]C NMR data are compiled in Table 2. λ_{max}^{MeOH} nm 225;

$$[\alpha]^{\lambda} \frac{589 \quad 578 \quad 546 \quad 436}{-33.84 \quad -35.2 \quad -40.57 \quad -88.82} (CHCl_3;\ c\,4.5)$$

Compound **2a**. Colourless oil, HRMS calc. for $C_{22}H_{28}O_5$ MW: 372.1937, found M_r (MS) 372.1933. IR ν_{max}^{KBr} cm^{-1}: 3600–3300, 1740, 1680, 875, 780. The [1]H and [13]C NMR data of **2a** are showed in Tables 1 and 2, respectively. Compound **2a** was esterified with CH_2N_2 in Et_2O, to give **2b** as a colourless oil. UV λ_{max}^{MeOH} nm 298; $\lambda_{max}^{n-hexane}$ nm 292.

$$[\alpha]^{\lambda} \frac{589 \quad 578 \quad 546 \quad 436}{-122.31 \quad -128.71 \quad -152.33 \quad -333.54} (CHCl_3;\ c\,0.619)$$

MS m/z (rel. int.) 386 $[M]^+$ (1.4), 354 $[M-MeOH]^+$ (2.8), 313 $[M-73]^+$ (75); 281 $[354-73]^+$ (44.2); 95 $[C_6H_7O]^+$ (27.1); 81 $[C_5H_5O]^+$ (100).

See Tables 1 and 2 for [1]H and [13]C NMR data respectively.

The treatment of **2a** with methanolic KOH gave **2c**. See [1]H NMR in Table 1.

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TRITERPENES FROM *CIGARRILLA MEXICANA**

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Key Word Index—*Cigarrilla mexicana*; Rubiaceae; cucurbitacin E; isocucurbitacin B; *epi*-isocucurbitacin B; 3β-23-dihxdroxy-urs-12-en-28-oic-acid; cucurbitacins.

Abstract—From the aerial parts of *Cigarrilla mexicana* 3β, 23-dihydroxy-urs-12-en-28-oic acid, a new natural product, has been isolated together with the already known cucurbitacin E, isocucurbitacin B, *epi*-isocucurbitacin B, ursolic and oleanoic acids. The structure of the new substance was established by chemical and spectroscopic means.

INTRODUCTION

In continuation of our work on Mexican plants used in Traditional Medicine, we have now investigated aerial parts of *Cigarrilla mexicana* (Zucc *et* Martius *ex* DC) Aiello (Rubiaceae), known in Mexico as cigarro, cigarrilla or cacaloxochilt. Cigarrilla is a monotypic species endemic to Hidalgo, Querétaro and San Luis Potosí, Mexico. The aerial parts, intensely bitter, are used locally for the treatment of amebiasis and as an emetic [1; Lorence, D., unpublished results]. No previous chemical work on the plant has been described.

RESULTS AND DISCUSSION

After repeated column chromatography on silica gel the concentrated methanolic extract of the defatted aerial parts of *C. mexicana* afforded the known compounds cucurbitacin E, isocucurbitacin B, *epi*-isocucurbitacin B as well as oleanoic and ursolic acids. In addition, a new natural ursene **1**, was isolated in 0.006% yield.

Compound **1**, $C_{30}H_{48}O_4$, mp 266–268°, was obtained as colourless needles. Treatment of **1** with pyridine–acetic anhydride afforded diacetate **1b** and methylation with diazomethane yielded methylester **1a**. Finally, treatment with acetone–H_2SO_4 gave the stable acetonide **1c**, thus indicating the presence of a 1–3 or 1–2 glycol moiety in the molecule.

The electron impact mass spectrum showed ions at m/z 248 (base), 223, 205 [223 $-H_2O$] and 203 [248 $-$COOH], the typical retro-Diels–Alder fragments of a triterpene acid of the Δ^{12} oleanene or ursane type [2, 3]. Furthermore the peaks at m/z 223 and 205 indicated that **1** had two hydroxyl groups on the ring A and/or ring B [4].

The ^{1}H NMR spectrum of **1** (Table 1) exhibited signals for two secondary methyl groups, four methyl singlets, one proton doublet ($J = 11$ Hz) at δ 2.17 (H-18) and one proton multiplet at δ 5.20 (H-12), as expected for an urs-12-ene skeleton [5–7]. Also, it showed an AB system (δ 3.29, 3.65, $J = 11$ Hz), which s ifted downfield on acylation in **1b**, indicative of the presence of an equat rial hydroxy methylene group attached to an asymmetric

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